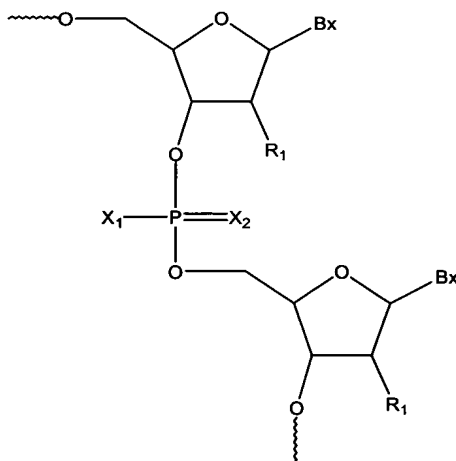


This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently amended) A method of preparing an oligomeric compound having at least one moiety of formula:



wherein:

$X_2$  is O or S;

$X_1$  is Pg-O-, Pg-S-,  $C_1$ - $C_{10}$  straight or branched chain alkyl,  $CH_3(CH_2)_{nn}$ -O-,  $R_2R_3N$ - or a group remaining from coupling a chiral auxiliary;

$nn$  is from 0 to 10;

Pg is  $CH_3$ ,  $-CH_2CH_2CN$ ,  $-C(CH_3)(CH_3)-CCl_3$ ,  $-CH_2-CCl_3$ ,  $-CH_2CH=CH_2$ ,  $CH_2CH_2SiCH_3$ , 2-yl-ethyl phenylsulfonate,  $\delta$ -cyanobutenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

$R_1$  is, independently, hydrogen, a blocked hydroxyl group, or a sugar substituent group, ~~a nitrogen protecting group, a substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, a substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, or a substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl,~~

wherein said substitution is ~~OR<sub>3</sub>, SR<sub>3</sub>, NH<sub>3</sub><sup>+</sup>, N(R<sub>3</sub>)(R<sub>4</sub>), guanidine or acyl where said acyl is an acid amide or an ester;~~

R<sub>2</sub> is, independently, hydrogen, a C<sub>1</sub>-C<sub>10</sub> alkyl, a cycloalkyl, or an aryl, ~~a nitrogen protecting group, a substituted or unsubstituted C<sub>4</sub>-C<sub>10</sub> alkyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, or a substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, wherein said substitution is OR<sub>3</sub>, SR<sub>3</sub>, NH<sub>3</sub><sup>+</sup>, N(R<sub>3</sub>)(R<sub>4</sub>), guanidine or acyl where said acyl is an acid amide or an ester;~~

~~or R<sub>1</sub> and R<sub>2</sub> together, are a nitrogen protecting group or are joined in a ring structure;~~

R<sub>3</sub> is, independently, hydrogen, a C<sub>1</sub>-C<sub>10</sub> alkyl, a cycloalkyl, or an aryl, ~~or a nitrogen protecting group;~~

R<sub>4</sub> is, independently, N(L<sub>1</sub>)L<sub>2</sub> ~~hydrogen, a C<sub>4</sub>-C<sub>10</sub> alkyl, or a nitrogen protecting group;~~

~~or R<sub>3</sub> and R<sub>4</sub>, together, are a nitrogen protecting group;~~

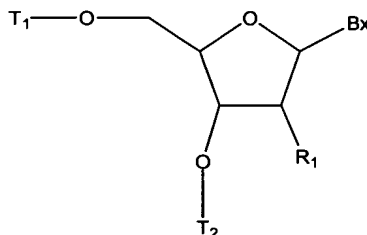
~~or R<sub>3</sub> and R<sub>4</sub> are joined in a ring structure;~~

or optionally, R<sub>2</sub> and R<sub>3</sub>, together with the nitrogen atom to which they are attached form a cyclic moiety;

each Bx is, independently, a heterocyclic base moiety; and

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



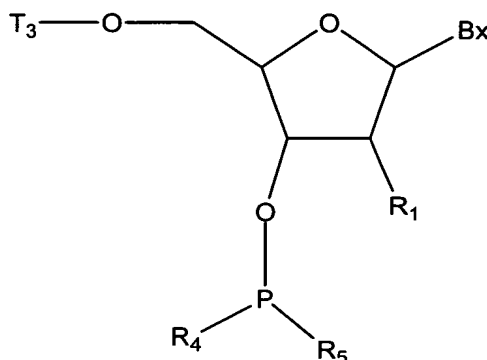
wherein:

T<sub>1</sub> is a hydroxyl protecting group; and

T<sub>2</sub> is a covalent attachment to a support media, a nucleoside bound to a support media, a nucleotide, an oligonucleoside or an oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:



wherein:

T<sub>3</sub> is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

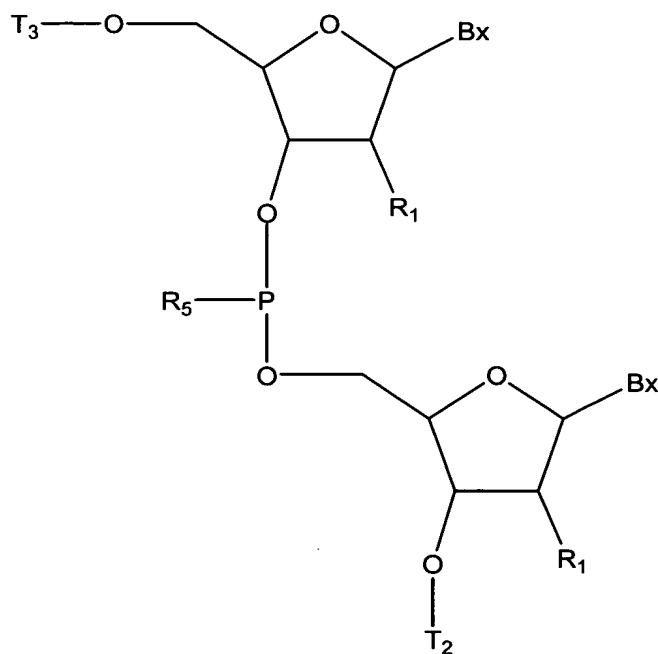
each L<sub>1</sub> and L<sub>2</sub> is, independently, C<sub>1-6</sub> straight or branched alkyl, or a C<sub>5-7</sub> cyclic aliphatic ring system;

or L<sub>1</sub> and L<sub>2</sub> are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which L<sub>1</sub> and L<sub>2</sub> are attached; and

R<sub>5</sub> is X<sub>1</sub>;

or R<sub>4</sub> and R<sub>5</sub> together with the phosphorus atom to which R<sub>4</sub> and R<sub>5</sub> are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having the formula:



(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent in a single step and for a time and under conditions effective to form said oligomeric compound, and

(e) treating said oligomeric compound with a reagent for a time and under conditions effective to remove said blocking groups thereby forming a deblocked oligomeric compound.

2. Canceled

3. (Previously presented) The method of claim 1 wherein said reagent in step (e) is effective to cleave the oligomeric compound from the support media.

4. (Previously presented) The method of claim 3 wherein said reagent in step (e) is aqueous ammonium hydroxide.

5. (Previously presented) The method of claim 1 further comprising treating said oligomeric compound with a further reagent for a time and under conditions effective to cleave the oligomeric compound from the support media.

6. (Original) The method of claim 1 further comprising treating said oligomeric compound with a deprotecting reagent for a time and under conditions effective to deprotect the T<sub>3</sub> hydroxyl protecting group.

7. (Original) The method of claim 1 wherein said mixture comprises from 0.02M to 0.2M oxidizing reagent.

8. (Original) The method of claim 7 wherein said mixture comprises from 0.1M to 0.2M oxidizing reagent.

9. (Original) The method of claim 1 wherein said oxidizing reagent transfers an oxygen atom.

10. (Original) The method of claim 9 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, tetra-*n*-butylammonium periodate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, cumene hydroperoxide, hydrogen peroxide; bis-

trimethylsilyl peroxide; dinitrogen tetroxide, oxone, molecular oxygen, (1*S*)-(+)-(10-camphorsulfonyl)oxaziridine or a peracid.

11. (Original) The method of claim 10 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, hydrogen peroxide, oxone, molecular oxygen or a peracid.

12. (Original) The method of claim 1 wherein said oxidizing reagent transfers a sulfur atom.

13. (Original) The method of claim 12 wherein said oxidizing reagent is 3-amino-1,2,4-dithiazole-5-thione; 3-ethoxy-1,2,4-dithiazoline-5-one; 1,2,4-dithiazolidine-3,5-dione; 3-methyl-1,2,4-dithiazolin-5-one; or dimethylthiuram disulfide.

14. (Original) The method of claim 13 wherein said oxidizing reagent is dimethylthiuram disulfide.

15. (Original) The method of claim 1 wherein said capping reagent comprises about one part by volume of either acetic anhydride in acetonitrile or tetrahydrofuran; or chloroacetic anhydride in acetonitrile or tetrahydrofuran; added to about one part by volume of either N-methylimidazole and pyridine in acetonitrile or tetrahydrofuran; or *t*-butylphenoxyacetic anhydride in acetonitrile or tetrahydrofuran.

16. (Original) The method of claim 15 wherein said capping reagent comprises about one part by volume of 20% acetic anhydride in acetonitrile mixed with about one part by volume of a solution having 20% N-methylimidazole, 30% pyridine and 50% acetonitrile.

17. (Original) The method of claim 1 wherein said mixture comprises dimethylthiuram disulfide, acetic anhydride, acetonitrile, N-methyl imidazole and pyridine.

18. (Original) The method of claim 1 wherein said mixture comprises from about 0.05M to 0.2M dimethylthiuram disulfide, about 10% acetic anhydride, about 10% N-methyl imidazole and about 15% pyridine in a suitable solvent.

19. (Original) The method of claim 18 wherein said solvent is acetonitrile, toluene, ethyl acetate, tetrahydrofuran, dichloromethane, dichloroethane, dioxane, dimethylacetamide and dimethylformamide.

20. (Original) The method of claim 1 wherein said coupling of the 5'-O-deprotected compound with the activated phosphorus composition is performed in the presence of an activating agent.

21. (Original) The method of claim 20 wherein said activating agent is 1-H-tetrazole or 4,5-dicyanoimidazole.

22. (Original) The method of claim 1 where said cyclic moiety is morpholino or phthalimido.

23. (Original) The method of claim 1 wherein each  $L_1$  and  $L_2$  is  $C_{1-6}$  alkyl.
24. (Original) The method of claim 23 wherein each  $L_1$  and  $L_2$  is isopropyl.
25. (Original) The method of claim 1 wherein  $L_1$  and  $L_2$  are joined together to form a heterocyclic ring system including the nitrogen atom to which said  $L_1$  and  $L_2$  are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S.
26. (Original) The method of claim 25 wherein said heterocyclic ring system is morpholino.
27. Canceled.
28. (Original) The method of claim 1 wherein said  $X_1$  is Pg-O-, Pg-S-,  $CH_3$ -,  $CH_3$ -O-, morpholino or  $R_2R_3N$ - where each  $R_2$  and  $R_3$  is, independently, hydrogen or  $C_1$ - $C_{10}$  alkyl.
29. (Original) The method of claim 1 wherein said Pg is  $CH_2CH_2CN$ , diphenylsilylethyl,  $\delta$ -cyanobutenyl, cyano p-xylyl, methyl-N-trifluoroacetyl ethyl or acetoxo phenoxy ethyl.



30. (Original) The method of claim 1 wherein said heterocyclic base moiety is adenine, N<sup>6</sup>-benzoyladenine, cytosine, N<sup>4</sup>-benzoylcytosine, 5-methylcytosine, N<sup>4</sup>-benzoyl-5-methylcytosine, thymine, uracil, guanine, N<sup>2</sup>-isobutyrylguanine or 2-aminoadenine.

31. (Original) The method of claim 1 wherein said support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide is blocked at reactive sites.

32. (Original) The method of claim 1 wherein said blocking groups are acid stable.

33. (Original) The method of claim 1 wherein said blocking groups are base labile.

34. (Original) The method of claim 1 wherein said deprotecting reagent is acidic, neutral or basic.

35. (Currently amended) The method of claim 34 wherein said deprotecting reagent is dichloroacetic acid, trichloroacetic acid, zinc bromide, AlCl<sub>3</sub>, TiCl<sub>4</sub>, (Et)AlCl, ~~(*i*-Bu)<sub>2</sub>AlCl~~, (*i*-Bu)<sub>2</sub>AlCl, ceric ammonium nitrate, 1,1,1,3,3,3-hexafluoro-2-propanol or diethyloxomalonate.

36. (Original) The method of claim 35 wherein said deprotecting reagent is 2-5% dichloroacetic acid in dichloromethane or dichloroethane.

37. (Original) The method of claim 1 wherein said deprotecting reagent is a fluoride moiety.

38. (Original) The method of claim 37 wherein said fluoride moiety is  $\text{BF}_3$ -etherate.

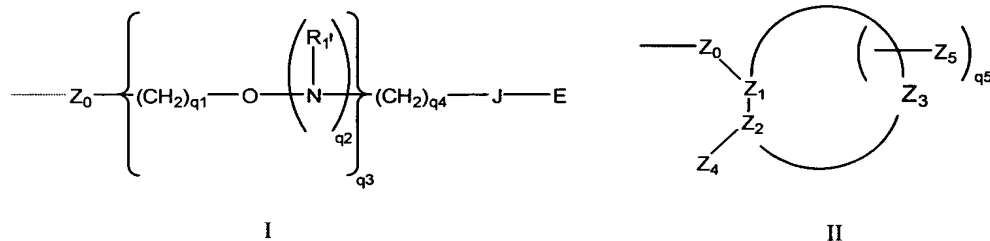
39. (Original) The method of claim 1 wherein said oligomeric compound comprises from 5 to about 50 nucleosides.

40. (Original) The method of claim 1 wherein said oligomeric compound comprises from 8 to about 30 nucleosides.

41. (Original) The method of claim 1 wherein said oligomeric compound comprises from 15 to about 25 nucleosides.

42. (New) The method of claim 1 wherein each of said sugar substituent groups is, independently,  $\text{C}_1$ - $\text{C}_{20}$  alkyl,  $\text{C}_2$ - $\text{C}_{20}$  alkenyl,  $\text{C}_2$ - $\text{C}_{20}$  alkynyl,  $\text{C}_5$ - $\text{C}_{20}$  aryl, O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, O-alkylamino, O-alkylaminoalkyl (O-alkyl-N(H)alkyl), O-alkylaminodialkyl (O-alkyl-N-(alkyl)<sub>2</sub>), O-alkylalkoxy (O-alkyl-O-alkyl), O-alkyl-(N-imidazole), thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, S-aryl, NH-aryl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, N-imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, or polyether;

or, alternatively, one or more substituent groups has one of formula I or II:

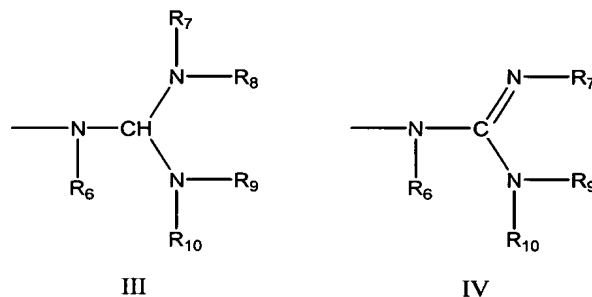


wherein:

$Z_0$  is O, S or NH;

J is a single bond, O or C(=O);

E is  $C_1$ - $C_{10}$  alkyl,  $N(R_1')(R_2')$ ,  $N(R_1')(R_5')$ ,  $N=C(R_1')(R_2')$ ,  $N=C(R_1')(R_5')$  or has one of formula III or IV;



each  $R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$  and  $R_{10}$  is, independently, hydrogen,  $C(O)R_{11}$ , substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally,  $R_7$  and  $R_8$ , together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, R<sub>9</sub> and R<sub>10</sub>, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R<sub>11</sub> is, independently, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R<sub>5'</sub> is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a support media;

each R<sub>1'</sub> and R<sub>2'</sub> is, independently, H, a nitrogen protecting group, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, wherein said substitution is OR<sub>3</sub>, SR<sub>3</sub>, NH<sub>3</sub><sup>+</sup>, N(R<sub>3'</sub>)(R<sub>4'</sub>), guanidino or acyl where said acyl is an acid amide or an ester;

or R<sub>1'</sub> and R<sub>2'</sub>, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or R<sub>1'</sub>, T and L, together, are a chemical functional group;

each R<sub>3'</sub> and R<sub>4'</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, a nitrogen protecting group, or R<sub>3'</sub> and R<sub>4'</sub>, together, are a nitrogen protecting group;

or R<sub>3'</sub> and R<sub>4'</sub> are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

Z<sub>4</sub> is OX, SX, or N(X)<sub>2</sub>;

each X is, independently, H, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> haloalkyl, C(=NH)N(H)R<sub>5'</sub>, C(=O)N(H)R<sub>5'</sub> or OC(=O)N(H)R<sub>5'</sub>;

R<sub>5'</sub> is H or C<sub>1</sub>-C<sub>8</sub> alkyl;

$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(R_1)(R_2)$ ,  $OR_1$ , halo,  $SR_1$ , or CN;

each  $q_1$  is, independently, an integer from 1 to 10;

each  $q_2$  is, independently, 0 or 1;

$q_3$  is 0 or an integer from 1 to 10;

$q_4$  is an integer from 1 to 10;

$q_5$  is from 0, 1 or 2; and

provided that when  $q_3$  is 0,  $q_4$  is greater than 1.